

In the Specification

Please substitute the following paragraph on page 45, beginning at line 1:

For amplification purposes, pairs of primers with approximately the same  $T_m$  are preferable. Primers may be designed using the OSP software (Hillier and Green, 1991), the disclosure of which is incorporated by reference in its entirety, based on GC content and melting temperatures of oligonucleotides, or using PC-Rare (<http://www.bioinformatics.weizmann.ac.il/software/PC-Rare/doc/manuel.html>) based on the octamer frequency disparity method (Griffais *et al.*, 1991), the disclosure of which is incorporated by reference in its entirety. DNA amplification techniques are well known to those skilled in the art. Amplification techniques that can be used in the context of the present invention include, but are not limited to, the ligase chain reaction (LCR) described in EP-A-320 308, WO 9320227 and EP-A-439 182, the polymerase chain reaction (PCR, RT-PCR) and techniques such as the nucleic acid sequence based amplification (NASBA) described in Guatelli *et al.* (1990) and in Compton (1991), Q-beta amplification as described in European Patent Application No 4544610, strand displacement amplification as described in Walker *et al.* (1996) and EP A 684 315 and, target mediated amplification as described in PCT Publication WO 9322461, the disclosures of which are incorporated by reference in their entireties.

Please substitute the following paragraph on page 68, beginning at line 26 through to page 69, line 13:

The polypeptides of SEQ ID NOs: 242-482 were screened for the presence of known structural or functional motifs or for the presence of signatures, small amino acid sequences that are well conserved amongst the members of a protein family. The search was conducted on the Pfam 5.5 database using HMMER-2.1.1 (for info see Sonnhammer et Durbin, <http://www.sanger.ac.uk/Pfam/>), on a Blocks Plus database containing Blocks version 12.6, Prints version 26.0, Pfam version 5.3, Prodom version 99.1, and Domo version 2.0 using emotif (for info see Nevill-Manning *et al.*, *PNAS*, 95, 5865-5871, (1998), <http://motif.stanford.edu/EMOTIF>) and on the Prosite 16.0 database using bla (Tatusov, R. L. & Koonin,

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E. V. CABIOS 10, No. 4) and pfscan ([http://www. Worldwide Website: isrec.isb-sib.ch/cgi-bin/man.cgi?section=l&topic=pfscan](http://www.Worldwide-Website.isrec.isb-sib.ch/cgi-bin/man.cgi?section=l&topic=pfscan)). Some of these predicted domains are described in Table VI. For these polypeptides referred to by their sequence identification numbers (column entitled "Seq Id No"), Table VI gives the designation of the domain (column entitled "Designation of domain") according to the database of domains indicated in the column entitled "Database" and the positions of preferred fragments within these sequences (column entitled "Positions of domains"). Each fragment is represented by a-b where a and b are the start and end positions respectively of a given preferred fragment on the full-length polypeptide. Preferred fragments are separated from each other by a comma. As used herein, the term "domain described in Table VI" refers to all the domains listed in Table VI for a given GENSET protein referred to by its sequence identification number in the first column. It should be noted that in Table VI, the first methionine encountered is designated as amino acid number 1, i.e; the leader sequence is not numbered negatively. In the appended sequence listing, the first amino acid of the mature protein resulting from cleavage of the signal peptide is designated as amino acid number 1 and the first amino acid of the signal peptide is designated with the appropriate negative number, in accordance with the regulations governing sequence listings.

Please substitute the following paragraph on page 280, beginning at line 25 through to page 281, line 2:

The protein of SEQ ID NO:297 is a splice variant of synaptogyrin 1. The splicing of the cDNA of SEQ ID NO:56 is different for exon 3: whereas exon 3 of synaptogyrin 1 is 238 base-pair long, exon 3 of SEQ ID NO:56 is 345 base-pair long. This introduces a frameshift and a stop codon. Thus, the protein of SEQ ID NO:297 is identical to synaptogyrin 1 up to and including amino acid ~~122~~ 112, the remaining 22 amino acids are entirely different. When compared to synaptogyrin 1, the protein of the invention presents the same N-terminal domain (which is highly conserved in all synaptogyrins) and 2 of the 4 transmembrane helices. Preferred polypeptides of the invention are those that comprise amino acids 1 to 16, which make up the N terminal cytoplasmic domain of the protein and which are highly conserved among all members of the synaptogyrin family (Kedra D et al.--Hum Genet.--1998, 103(2):131-141). Other preferred polypeptides of the invention are those

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that comprise amino acids 25 to 45 and/or 68 to 88, which make up the two transmembrane alpha helices. Thus it is believed that the protein of the invention is a member of the synaptogyrin family.

Please substitute the following paragraph on page 434, beginning at line 31 through to page 435, line 5:

Sequences within untranscribed or untranslated regions of polynucleotides of the invention may be identified by comparison to databases containing known regulatory sequence such as transcription start sites, transcription factor binding sites, promoter sequences, enhancer sequences, 5'UTR and 3'UTR elements (Pesole *et al.*, 2000; <http://www.igs-server.cnrs-mrs.fr/~gauthere/UTR/index.html>). Alternatively, the regulatory sequences of interest may be identified through conventional mutagenesis or deletion analyses of reporter plasmids using, for instance, techniques described in the section entitled "Identification of Promoters in Cloned Upstream Sequences".